Inert ingredient information may be entitled to confidential treatment

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 1 4 2005

MEMORANDUM

SUBJECT: Science Review to support registration of end use product (EP), **KEYPLEX 350 OR** (EPA Reg. No. 73512-U), containing 0.063 % w/w active ingredient **brewers yeast extract** from *Saccharomyces cerevisiae*, active ingredient (PC Code: 100053).
DP Barcode: DP 320658. Decision No. 351084.
MRDs: 466187-01; 465904-02; 466187-02.

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ACTION REQUESTED

Morse Enterprise Limited, Inc. is resubmitting data required for registration of end use product, **KEYPLEX 350 OR** (EPA Reg. No. 73512-U), containing 0.063 % w/w active ingredient **brewers yeast extract** from *Saccharomyces cerevisiae*. The proposed end product (EP) is similar in formulation to KeyPlex 350 (EPA Reg.No. 73512-1). The only difference between the currently proposed product, KeyPlex 350 OR, and the EPA registered KeyPlex 350 (EPA Reg. No. 73512-1) is that the [redacted] has been changed and several of the suppliers for the inert ingredients were changed. The active source material, Yeast Hydrolysate OR Liquid Manufacturing Use Product (EPA Reg. No. 73512-G), which is present in the proposed EP, is slightly different from the previously registered Manufacturing Use Product Yeast Hydrolysate Liquid (EPA Reg. No. 73512-2), used to manufacture the already registered product KeyPlex 350 (EPA Reg. No. 73512-1). The difference is that the [redacted] were removed from the Yeast Hydrolysate Liquid Manufacturing Use Product (EPA Reg. No. 73512-2). A registration application was recently submitted to EPA for the new manufacturing product (MP) (EPA reg. No. 73512-G) used to manufacture KeyPlex 350 OR (EPA Reg. No. 73512-U).

RECOMMENDATIONS AND CONCLUSIONS

The registrant resubmitted chemistry data, amended CSF, and updated rationale for waiving required mammalian toxicity, non-target organisms, and environmental fate studies in support of registration of new EP, **KEYPLEX 350 OR** (EPA Reg. No. 73512-U), containing 0.063 % w/w

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active ingredient **brewers yeast extract** from *Saccharomyces cerevisiae*. The active ingredient is from **MUP Yeast Hydrolysate OR** (EPA Reg. No. 73512-G), currently pending registration, which contains 2.50 % w/w active ingredient **brewers yeast extract** from *Saccharomyces cerevisiae*.

I. The **product chemistry data are acceptable** pending registration of the MUP, and correction of the names for the [redacted]n the CSF. The CSF listed two synonyms for most of the inerts, one of which was a general name, and a second that specified the [redacted] of the compound. Only one name should be provided on the CSF for each inert, with its corresponding CAS number.

II. The requested waivers for Tier I toxicity are **unacceptable** and pending registration of the MUP. This resubmission fails to cite **specific data** for **acute inhalation, and skin sensitization (guinea pig) studies** or **specific rationale** for waiving these data requirements. Waiver requests, as resubmitted, fail to cite study sources for Primary Dermal and Eye Irritation data.

III. Waiver requests, as resubmitted in MRID 465904-02, state the same results from a primary skin irritation study to satisfy separate data requirements for both, acute dermal and primary skin irritation studies. **This study must be cited**.

IV. Waiver requests, as resubmitted in MRID 465904-02, refer to results from a primary eye irritation study. **This study must be cited.**

V. **Waiver requests for all non-target organism toxicity studies are acceptable pending registration of the manufacturing use product (MUP) Yeast Hydrolysate OR** (EPA Reg. No. 73512-G), since these studies are not required for and end use product containing a registered source of active ingredient.

VI. **Waiver requests, as submitted, fail to address skin sensitization study.** Neither study nor data waiver requests are presented for Skin Sensitization (Guinea pig study) in this resubmission.

Table 1. Mammalian Toxicity Categories

Mammalian Toxicity Studies	Guideline	Study Results	Toxicity Categories
Acute Oral Toxicity	870.1100	LD_{50} > 5000 mg/kg; Intraperitoneal route: LD_{50} > 4500 mg/kg in rats, LD_{50} >8 g/kg in	IV CAUTION

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		mice	
Acute Dermal Toxicity	870.1200	No data	
* Primary Dermal Irritation	870.2500	Mild or very slight irritation in rabbits. (PDII) = 0.04	IV CAUTION
* Primary Eye Irritation	870.2400	no positive signs after 72 hours. Average MMTS = 3.3 (24 hrs.) 0.7 (48 hrs.)	III CAUTION
Skin sensitization-Guinea pig	870.2600	No data	no data
Acute Inhalation Toxicity	870.1300	No data	no data
Hypersensitivity Incidents		no adverse effects to users and workers found	

* These studies are not cited.

BACKGROUND AND REVIEWER COMMENTS

KeyPlex 350 OR is similar to KeyPlex 350 (EPA Reg. No. 73512-1), an end use product that contains an identical concentration (0.063%) of the same active ingredient. KeyPlex 350 OR uses a different manufacturing use product, Yeast Hydrolysate OR (EPA reg. No. 73512-G), for which a separate registration application has been submitted, to supply the active ingredient, and contains a different [redacted] as one of the inert ingredients. Also, some of the suppliers of the inerts in KeyPlex 350 OR are different from those used for KeyPlex 350.

Waiver requests for mammalian toxicity studies, as submitted, fail to specifically address acute inhalation, acute dermal toxicity, and skin sensitization (guinea pig) studies.

Waiver requests, as resubmitted, fail to cite study sources for Primary Dermal and Eye Irritation data. Ecological and non-target effects data are not required for an end use product (EP) containing a registered source of active ingredient. Furthermore, no adverse effects are expected on endangered and threatened species via use of this product according to label use directions. The NAA determination is based on: a) low to no mammalian toxicity (see Acute Toxicity Categories in Study summary below), b) lack of toxicity to non-target test organisms, c)

low application rate, d) rapid degradation of the active ingredeint, e) FDA GRAS status of the active ingredient, and f) the natural occurrence of the active ingredient in the environment.